ORAL BONIVA® (ibandronate sodium)
SUMMARY OF CLINICAL INFORMATION

FRACTURE EFFICACY - Background

- Ibandronate is indicated for the prevention and treatment of post-menopausal osteoporosis. In the pivotal fracture trial, BONE, ibandronate (IBN) reduced the relative risk of new vertebral fractures by 52%.[1] New moderate or severe vertebral fractures were reduced by 59% as early as the first year.[2]
- IBN daily reduced the risk of non-vertebral fractures (NVF) by 69% in a post-hoc analysis of higher risk patients in BONE (femoral neck T-score < –3; n=375).[1] In patients with a lumbar spine T-score <–2.5 and a history of clinical fractures in the previous 5 years, a significant 60% reduction in NVF was shown.[3]

NEW EFFICACY DATA

- Two separate meta-analyses of IBN clinical studies were conducted to assess the effect of different IBN doses on NVF. In these trials individual patient data were grouped into dose levels based on annual cumulative exposure [ACE]. ACE is calculated as the annual dose (mg) multiplied by the bioavailability (0.6% for oral and 100% for the IV formulation). For example, the ACE for the 2.5 mg daily dose is 2.5mg/day oral x 365 days x 0.006 = 5.5mg, whereas the ACE for the 150 mg monthly oral dose is 150 mg/month x 12 months x 0.006 = 10.8 mg. Both studies found that higher doses of IBN (defined as an annual cumulative exposure [ACE] ≥ 10.8 mg, significantly reduced the risk of NVF.[4,5] The currently marketed doses of IBN (Oral 150 mg monthly and IV 3mg quarterly) are included provide an ACE of ≥ 10.8 mg.

    - The Harris et al. meta-analysis included all 4 pivotal IBN trials (BONE, MOBILE, DIVA, MF4380) and assessed the fracture risk reduction of various doses relative to placebo. IBN ACE ≥ 10.8 mg decreased the risk of NVF by 30% compared with placebo.[4]

    - A second, independent meta-analysis by Cranney et al. included data from two pivotal studies of IBN (MOBILE, DIVA) and assessed the fracture risk reduction of various doses of IBN compared with the 2.5 mg dose. In this analysis dosages where IBN ACE ≥ 10.8 mg decreased the risk of NVF by 38% compared with the 2.5 mg daily dose.[5]

- The Evaluation of Ibandronate Efficacy Study (VIBE) was a large retrospective claims database study of >64,000 patients comparing fracture rates between patients treated with monthly IBN and weekly bisphosphonates (BPs) (alendronate [ALN] or risedronate).[6] At 1 year, the rates of hip and NVF were low with no significant differences between the 2 groups. Patients treated with IBN, however, had significantly fewer vertebral fractures than those treated with weekly BPs. These findings of NVF incidence are in agreement with previous meta-analyses and show monthly ibandronate has comparable efficacy to other bisphosphonates in a diverse population of patients treated in real world settings.[6]

ADDITIONAL EFFICACY AND SAFETY RESULTS

- The Monthly Oral Therapy with Ibandronate for Osteoporosis Intervention Study (MOTION) was a head-to-head non-inferiority study comparing the efficacy and safety of monthly IBN (150 mg) and weekly ALN (70 mg). After 1 year, IBN met the co-primary endpoints of non-inferiority vs ALN with regard to bone mineral density (BMD) gains at the lumbar spine and total hip. The respective BMD gains achieved at the lumbar spine were 5.1% vs 5.8%, and 2.9% vs 3.0% at the total hip. Additionally, there were no notable differences in the types or incidences of adverse events. With regard to BMD responder analysis, the response rate at the lumbar spine was 90% vs 92% for IBN and ALN respectively. The total hip BMD response rate was 87% vs 90% for IBN and ALN respectively.[7]

- The Monthly Oral Ibandronate in Ladies Study (MOBILE), Long-Term Extension trial, was a continuation of the non-inferiority study (MOBILE) of patients receiving 3 years of continuous treatment with monthly ibandronate.[8]
    - At 3 years, (MOBILE long term extension) IBN once-monthly produced consistent increases in lumbar spine BMD (7.6%) and was statistically significant from baseline. Furthermore, the monthly regimen produced statistically significant increases in BMD at the femoral neck, total hip, and trochanter, 3.5%, 4.1%, and 6.2% respectively.
    - Serum C-telopeptide of the alpha chain of type I collagen (sCTX) suppression continued throughout the long term extension with a median decrease of 83.3% (peak suppression level) for the 150 mg monthly dose. All sCTX levels remained within the normal premenopausal range.
    - IBN once-monthly was well-tolerated throughout the 3 years of continuous treatment. There was no serious upper GI AEs reported.

NEW PERSISTENCE DATA

- Data from 2 large independent medical claims databases, i3Innovus and Healthcore, found that, in a real-world setting, women receiving once monthly oral IBN have significantly greater persistence with therapy at 12 months compared with women receiving weekly oral BPs (alendronate or risedronate).[9]
- The i3Innovus database study showed that monthly users of IBN were 25% ($P<0.001$) less likely to discontinue therapy than weekly BP users. Similar results were observed in the Healthcore database analysis were monthly IBN users were 38% ($p<0.001$) more likely to stay on therapy than weekly users.[9]

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